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(54) Title: MOTION SICKNESS SPRAY COMPOSITION AND METHOD

(57) Abstract

A method of providing a person subject to a sudden turbulent motion protection from motion sickness which comprises spraying into the nasal passages of said person a sufficient amount of scopolamine whereby said person is protected from said motion sickness upon the entry of said scopolamine into the bloodstream of said patient.

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MOTION SICKNESS SPRAY COMPOSITION AND METHOD

Scopolamine has been proposed as an anti-motion sickness remedy, with recent efforts having been made to provide a transdermal administration of scopolamine as proposed by Chandrasekaren et al in Robinson, ed., Sustained and Controlled Release Drug Delivery Systems, "Transdermal Systems", pp. 579-582 [New York: Marcel Dekker, Inc. (1978)]. While oral or transdermal systems may be provided to deliver scopolamine to a person for motion sickness, there is necessarily a delay before the effective entry of the scopolamine into the person's bloodstream. In the case of a sudden air or water turbulence, a person who has not anticipated the need for a motion sickness remedy may suddenly find himself in a situation where he feels an instant need for such a remedy. This is particularly the situation where there is a group of persons confined in a relatively small space such as an airplane or a crowded boat or ship, where a sudden turbulence develops and then one person shows the extreme manifestation of motion sickness, that creates an often "contagious" need for fellow travellers to seek relief through the taking of a fast acting remedy. Tablets or transdermal remedies are not entirely satisfactory particularly where a fast relief is needed. In addition, the inconvenience of such forms should be noted. For example, the pilot of a small airplane suddenly facing severe air turbulence cannot go to the bathroom to obtain a glass of water with which to wash down a tablet, and a transdermal form would be obviously unsuited for very quick relief.

In accordance with the invention, it has been discovered that an aerosol spray composition is particularly suited for providing quick relief from motion sickness, and also for providing protection against motion sickness for a period that is normally desired for air travel, e.g., up to about three hours. The aerosol spray composition is administered by spraying into the nostrils of the person requiring the quick protection. Through administration via the nasal passages the scopolamine reaches the bloodstream in a rapid manner, far more quickly than through oral or transdermal application. Scopolamine administered through the aerosol spray composition of the invention may be advantageously used by persons who feel that they normally do not need a motion sickness remedy, but when a "panic" situation of sudden extreme air turbulence or particularly stormy conditions at sea arise, feel that they need protection. With tablets, it is recognized that a person should generally take the motion sickness remedy prior to the start of a voyage. If no conditions of extreme storminess arise, then the person has needlessly taken the drug, a condition of psychological drug dependence being fostered. By being able to rely upon the aerosol spray composition of the invention to provide very quick action, persons susceptible to motion sickness may avoid routine use of motion sickness drugs, but have a quick possibility for relief in a convenient form available.

The aerosol spray composition of the invention comprises a sufficient amount of scopolamine in a form suitable for nasal administration in a major amount of an aerosol spray vehicle suitable for nasal administration. The scopolamine in a form suitable for nasal administration may be scopolamine hydrochloride. As an example of an aerosol spray vehicle of the invention may be mentioned an aqueous solution which contains about 20% ethanol. In determining the amount

of scopolamine that should be included, the amount of spray that is to be used per dosage is to considered. With a sophisticated nasal spray aerosol delivery device, a small total amount of spray with a relatively higher concentration of scopolamine may be used whereas with a relatively unsophisticated metering capability a larger amount of spray with a relatively lower concentration should be used. In experiments a relatively simple nasal spray that is used for common nasal over the counter drugs has been sued. (A nasal spray device of the type used for selling "4-Way" spray was used in such experiments.)

The following examples serve to further illustrate the invention:

EXAMPLE I

An aerosol spray composition is prepared by first making a stock solution of 1000 ml which contains 20% of ethanol and the remainder water. 1 mg scopolamine hydrochloride is dissolved into 99.9 ml of the stock solution, which after dissolution constitutes an aerosol spray composition of the invention.

EXAMPLE II

15 ml of the aerosol spray composition produced via the procedure of Example I is placed into "4-Way" spray container. The aerosol spray composition is administered by shooting into each nostril, which is about 50 mg total aerosol spray composition for each nostril, resulting in a total delivery of scopolamine of about 100 micrograms. The person receives a relatively quick action of the scopolamine through this method, and sustained relief for a period of about three hours.

EXAMPLE III

By substituting 200 ml of the stock solution in Example I in place of the 100 ml stock solution used in that example, a more dilute aerosol spray composition is obtained. When the resultant aerosol spray composition thus produced is used in the procedure of Example II,

two "squirts" into each nostril is used to provide the same dosage level of scopolamine. This method is preferred when the nasal spray deliver device is not as sophisticated as some, and provides a more even dosage.

EXAMPLE IV

A 29 year old male scuba diving and seamanship instructor uses 0.3mg capsules of scopolamine (Tryptone) before sea trips in rough weather because he frequently becomes motion sick. He reports that the Tryptone capsules are effective in preventing not only nausea and vomiting but also the malaise that preceeds his motion sickness. On approximately ten occasions he has used intranasal scopolamine; two squirts in each nostril. He reports that, at first he administered this medicine prior to boarding the boat because he was unsure about the rapidity of onset. However, most of his experience with intranasal scopolamine has been after rough seas have been encountered. He reports that intranasal scopolamine has been effective in preventing all motion sickness symptoms. The onset of effect is within ten minutes and the duration of effect is at least five hours.

EXAMPLE V

A 30 year old female has used intranasal scopolamine on three occasions. Her previous experience with motion sickness remedies has been with the antihistamine, Dramamine. She found this medicine to have slow onset of effect and it seemed to produce a therapeutic effect only because it made her fall asleep. On the first administration of intranasal scopolamine, she had been riding in a boat for over an hour in five foot seas. She felt nauseous and fatigued and administered one squirt of scopolamine into each nostril. Within 15 minutes, the nausea had disappeared and she felt more alert. However, one hour later she notice dry mouth and her sleepiness had returned. The dry mouth was bothersome especially when she went scuba

diving because it became difficult to swallow; a technique necessary to equalize pressure in the ears and sinus while descending in the water. These symptoms lasted for 8 hours. On the second and third applications, she reduced the dose to one squirt, experienced the same relief of symptoms without the side effects.

EXAMPLE VI

A sixteen year old student had taken a boat trip as part of a scuba dive instruction class. With 10mph winds and 3 foot seas, he became violently ill (pallor, sweating, fatigue, retching and vomiting) 40 minutes after boarding the boat. Two days later, he went out in the same boat when seas were 4-5 feet high. He administered two squirts of intranasal scopolamine as he boarded the boat and developed no motion sickness symptoms. He reported no side effects.

EXAMPLE VII

A seventeen year old student who reported that he always become ill while riding o boats, used two squirts of intranasal scopolamine on two occasions while riding in a boat on days with 3-5 foot seas. On neither occasion did he experience any symptoms of motion sickness except for some sleepiness. No side effects occurred. The sleepiness could have been the prelude of motion sickness or an effect of scopolamine.

EXAMPLE VIII

A sixteen year old student had vomited on one occasion while riding on a boat. He used four squirts of intranasal scopolamine after boarding a boat to spend three hours in 4-6 foot seas. He developed no symptoms of sea sickness except some facial pallor despite the fact that his diving buddy vomited.

EXAMPLE IX

A 26 year old male vomited while surfacing from a 90 foot scuba dive. He had looked ill before descending on the dive and reported that he had felt nauseous. He

then used two squirts of scopolamine, laid down to rest and, in 30 minutes, reported that he felt well enough to make a second dive. He descended without problem and after surfacing, said he felt no nausea. His appearance was also much improved. He reported no side effects.

EXAMPLE X

A 40 year old female spent 1.5 hours on a boat in 6 foot seas. About 15 minutes before boarding the boat she used 2 squirts of intranasal scopolamine. A friend who accompanied her used no medication. During this sea trip, AT experienced only slight epigastric discomfort and no side effects. Her friend, however, became very ill and vomited repeatedly.

EXAMPLE XI

A 45 year old female has a long history of motion sickness while flying. She has vomited on a number of occasions. Dramamine had been used in the past and always put her to sleep. She has used 2 squirts of intranasal scopolamine on over ten flights of 3 hours duration or less. No motion sickness has developed on these flights and dry mouth is the only side effect experienced. Furthermore, on occasions when she has forgotten to use scopolamine, her motion sickness returns, indicating that tolerance to the effects of motion has not occurred.

EXAMPLE XII

A fifty year old male reports that he vomits while flying and that current motion sickness remedies are of little benefit. He has used 2 squirts of intranasal scopolamine on approximately 10 occasions while flying. No motion sickness has developed following the use of intranasal scopolamine and dry mouth was the only side effect noticed.

WHAT IS CLAIMED IS:

1. A method of providing a person subject to a sudden turbulent motion protection form motion sickness which comprises spraying into the nasal passages of said person a sufficient amount of scopolamine whereby said person is protected from said motion sickness upon the entry of said scopolamine into the bloodstream of said patient.

2. A method of claim 1 wherein said scopolamine is delivered into said nasal passages in the form of a spray of scopolamine in an aqueous mixture.

3. A method of claim 1 wherein said scopolamine is in the form of scopolamine hydrochloride dissolved in an ethanolic solution.

4. An aerosol spray composition contained in a vehicle suitable for propelling said aerosol spray composition in droplet form from said vehicle into the nasal passages of a patient, said aerosol spray composition comprising scopolamine in a form suitable for nasal administration dissolved in an aqueous solution.

5. An aerosol spray composition of claim 4 wherein said aqueous mixture is an ethanolic solution.

6. An aerosol spray composition of claim 4 or 5 wherein said form suitable for nasal administration is the hydrochloride.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US82/00941

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int. Cl.[3] A61K 31/46
U.S. Cl. 424/265

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
U.S.	424/265

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [5]

Chemical Abstracts For Scopolamine, 1968 - 1981

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category [6]	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
X	US, A, 3,169,095, Published 9 February 1965, Thiel et al	1-6
X	US, A, 3,681,500, Published 1 August 1972, Zeile et al	1-6
A	US, A, 4,031,894, Published 28 June 1977, Urquhart et al	1-6
X	N, Cutting "Handbook of Pharmacology", 4th Edition, Published 1967 by A.C.C. (New York), See pages 538-541	1-6
X	N, Merck Index, 9th Edition, Published 1976, by Merck and Co. (Rahway, New Jersey, U.S.A.), pages 1088 and 1089, See paragraphs 8158 and 8159	1-6

* Special categories of cited documents: [15]

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"T" later document published on or after the international filing date or priority date and not in conflict with the application, but cited to understand the principle or theory underlying the invention

"X" document of particular relevance

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [9]
20 October 1982	02 NOV 1982
International Searching Authority [1]	**Signature of Authorized Officer [10]**
ISA/US	Donald Stanley